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Prevalence and Risk Factors for *Mycobacterium tuberculosis* Infection Among Adolescents in Rural South Africa

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Background. We aimed to estimate the prevalence of and explore risk factors for *Mycobacterium tuberculosis* infection among adolescents in a high tuberculosis (TB) and human immunodeficiency virus (HIV) prevalence setting.

Methods. A cross-sectional study of adolescents (10–19 years) randomly selected from a demographic surveillance area (DSA) in rural KwaZulu-Natal, South Africa. We determined *M tuberculosis* infection status using the QuantiFERON-TB Gold-plus assay. We used HIV data from the DSA to estimate community-level adult HIV prevalence and random-effects logistic regression to identify risk factors for TB infection.

Results. We enrolled 1094 adolescents (548 [50.1%] female); *M tuberculosis* infection prevalence (weighted for nonresponse by age, sex, and urban/rural residence) was 23.0% (95% confidence interval [CI], 20.6–25.6%). *Mycobacterium tuberculosis* infection was associated with older age (adjusted odds ratio [aOR], 1.37; 95% CI, 1.10–1.71, for increasing age-group [12–14, 15–17, and 18–19 vs 10–11 years]), ever (vs never) having a household TB contact (aOR, 2.13; 95% CI, 1.25–3.64), and increasing community-level HIV prevalence (aOR, 1.43 and 95% CI, 1.07–1.92, for increasing HIV prevalence category [25%–34.9%, 35%–44.9%, ≥45% vs <25%]).

Conclusions. Our data support prioritizing TB prevention and care activities in TB-affected households and high HIV prevalence communities.

Keywords. IGRA; latent *Mycobacterium tuberculosis* infection; risk factors.

As an airborne infection, the risk of *Mycobacterium tuberculosis* infection is determined, in part, by the risk of contact with individuals with infectious tuberculosis (TB) disease [1]. *Mycobacterium tuberculosis* infection in young children (<10 years) is used as a marker of recent transmission and to make inferences about transmission in the population [2, 3]. Compared to older children and adults, young children have limited social contacts and are more likely than older children and adults to be infected within the household [4–7]. However, empirical evidence from both epidemiologic and molecular studies in high TB prevalence settings has shown that household transmission accounts for only between 8% and 20% of all transmission [8–12].

Throughout adolescence, young people have increasing social contact with the wider community and thus increased risk of *M tuberculosis* exposure and infection [7, 13, 14]. This suggests that *M tuberculosis* infection in adolescents might be a more representative measure of community-wide transmission than *M tuberculosis* infection in young children (aged <10 years), but there are few population-based studies from sub-Saharan Africa. We aimed to determine the prevalence of and risk factors for *M tuberculosis* infection among adolescents in a high TB and human immunodeficiency virus (HIV) prevalence setting.

METHODS

Study Setting

The study was conducted in the southern part of the Africa Health Research Institute's demographic surveillance area (DSA), in uMkhanyakude district, KwaZulu-Natal, South Africa, which has a resident population of approximately 60 000 and an adult HIV prevalence estimated at 36.6% in 2016 [15].

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The annual notification rate of all TB cases in KwaZulu-Natal was 394 per 100 000 population in 2018 (Oral personal communication, March 2020).

Study Participants and Procedures

We randomly selected adolescents (aged 10–19 years) from the complete sampling frame of all residents (individuals reported as intending to spend the majority of nights at a household within the DSA). Between November 2017 and December 2018, the selected individuals were visited at home and invited to take part. Because this study was originally designed to estimate *M tuberculosis* incidence at 12 months among adolescents who were negative at baseline, adolescents reporting any history of treatment for active TB were excluded. A standard questionnaire was administered that included questions on Bacillus Calmette-Guérin (BCG) vaccination, history of lifetime household TB contact, admission to hospital, smoking (and passive smoking), alcohol intake, and history of HIV testing. All participants were examined for presence of BCG scars (documentation of immunizations was also checked) and were asked history of attendance (including frequency of attendance in the previous month; duration, and number of people present at the last visit) at relevant indoor gathering places (school, church, health facility, and public transport). Data were collected on electronic tablets using the REDCap application (Vanderbilt University, Nashville, TN) [16].

Participants who were not known to be HIV positive, or whose most recent negative HIV test was more than 3 months previously, were encouraged to check their HIV status via a rapid HIV test on a fingerpick blood sample. Those who declined rapid testing were offered the option of undergoing anonymized laboratory enzyme-linked immunosorbent assay (ELISA) for research purposes only (further details on HIV testing are presented in the Supplementary Material Section 1). Participants newly testing HIV positive, and those previously diagnosed with HIV but not on antiretroviral therapy (ART), were referred to initiate ART [17]. Participants with TB symptoms (any of cough [≥2 weeks, or any duration if HIV positive], fever, night sweats, or weight loss) were asked to submit sputum for Xpert MTB/RIF testing. Those unable to produce sputum were referred to their nearest clinic for further management in accordance with national guidelines [18].

Information extracted from the DSA database included previous HIV test results (for those aged ≥15 years) and household data including urban/rural location, number of residents, socioeconomic status (SES), and distance to the nearest clinic. Community HIV prevalence (for individuals ≥15 years) was calculated using 2017 surveillance data by means of a 2-dimensional Gaussian kernel density of 3-km search radius, based on previously described methods [19]. Thus, the HIV prevalence for each household was estimated based on the population and number of known HIV-positive individuals within this search radius superimposed across the household. The HIV prevalence estimates for each household were categorized into 4 groups based on the frequency distribution of HIV prevalence of all households in the study area. The lowest category was coded "1" and included households with HIV prevalence below 25%. The highest category was coded "4" and included households with HIV prevalence at least 45%.

Laboratory Procedures

Details of laboratory testing are provided in the Supplementary Material Section 1. Briefly, venous blood was tested for *M tuberculosis* infection using the QuantiFERON-TB Gold Plus (QFT-Plus) assay (QIAGEN, Hilden, Germany) according to the manufacturer's instructions [20]. Sputum samples were tested using Xpert MTB/RIF (Cepheid, Sunnyvale, CA) at Hlabisa district hospital laboratory.

Definitions

Mycobacterium tuberculosis infection was defined as interferon-gamma (IFN-γ) concentration ≥0.35 IU/mL (calculated as either TB1 or TB2 antigen minus nil) per the manufacturer's guideline [20]. Lifetime household TB contact was defined as either having lived in the same household as a person with TB disease for ≥2 weeks or having cared for a person with TB during the participant's lifetime based on information reported by the participant and the parent for participants aged 10–17 years. Detailed definitions for exposures are provided in the Supplementary Material Section 2.

Statistical Analysis

A sample size of 1100 was sufficient to estimate the prevalence of *M tuberculosis* infection of 50% with a precision of ±3% at 5% significance level. To account for nonparticipation (both inability to contact participants and refusal to participate), a total 1998 adolescents were selected.

To account for nonparticipation, the weighted *M tuberculosis* infection prevalence was calculated by multiplying the crude prevalence by the inverse of probability of participation in strata-defined age, sex, and urban/rural residence. Characteristics of individuals included in the analysis were compared with those who were selected but were not included (because of nonparticipation or missing results) using χ^2 tests. Random-effects logistic regression taking account of clustering within households was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for the association of *M tuberculosis* infection with potential risk factors. To account for the interrelationships between the potential risk factors, a hierarchical approach [21] with 3 levels (community, household, and individual) was used to build a multivariable model (Figure 1). First, community factors associated with the outcome at $P < .20$ on univariable analysis were retained in a core model. Next, household factors

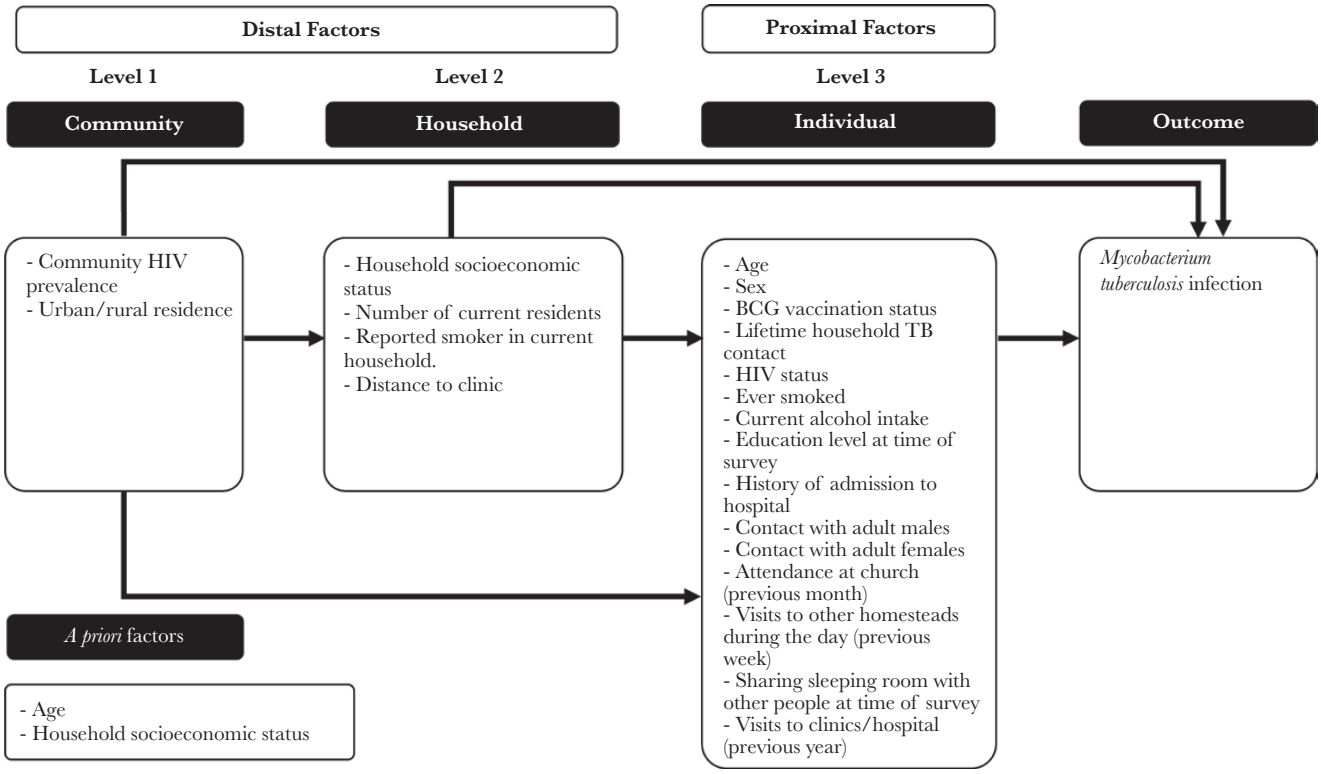

Figure 1 Conceptual framework for the hierarchical risk factor analysis for *M. tuberculosis* infection among adolescents

were added sequentially to the core model and retained if they remained associated with the outcome at $P < .20$ after adjusting for community factors and SES. Associations with individual-level factors were determined similarly, with age included in all the models as an a priori confounder. A complete case analysis was performed. Analyses were performed using Stata version 14.2 (College Station, TX).

Patient Consent Statement

The study was approved by the London School of Hygiene & Tropical Medicine Ethics Committee (ref. 10515), the Biomedical Research Ethics Committee of the University of KwaZulu-Natal (ref. BE483/15), and the KwaZulu-Natal Department of Health (ref. 184/16). Individual informed written consent was obtained from participants aged 18–19 years and from parents/guardians of participants aged 10–17 years, with informed assent from the participant. For participants or parent/guardians who could not read and/or write, a witness who was not a member of the research team attested to the informed consent procedure.

RESULTS

Participant Enrollment

Field workers successfully visited the homes of 1809 of 1998 (90.5%) selected individuals (Figure 2); 1173 of 1809 (64.8%) were screened for eligibility, 575 (31.8%) were not found, and 61 (3.4%) refused participation. Among those screened, 35 (3.0%) had a history of previous or current TB treatment, 3 (0.2%) were ineligible after crosschecking their date of birth, and the remaining 1135 (96.8%) were enrolled. The QFT-plus results were available for 1094 participants (Figure 2).

Individuals included in the analysis compared with those not included were more likely to be from rural communities and from communities with lower HIV prevalence (Supplementary Table 1). There were no differences by age, sex, or SES.

Among 1094 participants, 548 (50.1%) were female, 266 (24.4%) had a lifetime household TB contact, 379 (34.6%) were from urban communities, 965 (88.6%) had evidence of BCG vaccination, and 43 (3.9%) were HIV positive (Table 1). The median distance to the nearest clinic was 2.7 km (interquartile range, 1.7–4.2). Overall, 898 participants had a known HIV status: 641 were through testing in the study, 103 through surveillance activities, and 154 through self-reporting.

Mycobacterium tuberculosis Infection Prevalence

Two hundred forty-nine participants had IFN-γ values ≥0.35 IU/mL, giving a crude *M tuberculosis* infection prevalence of 22.8% (95% CI, 20.4%–25.3%). The *M tuberculosis* infection prevalence weighted for nonparticipation by age, sex, and rural/urban residence was 23.0% (95% CI, 20.6%–25.6%). The distribution of IFN-γ values for all participants is presented in Supplementary Figure 1.

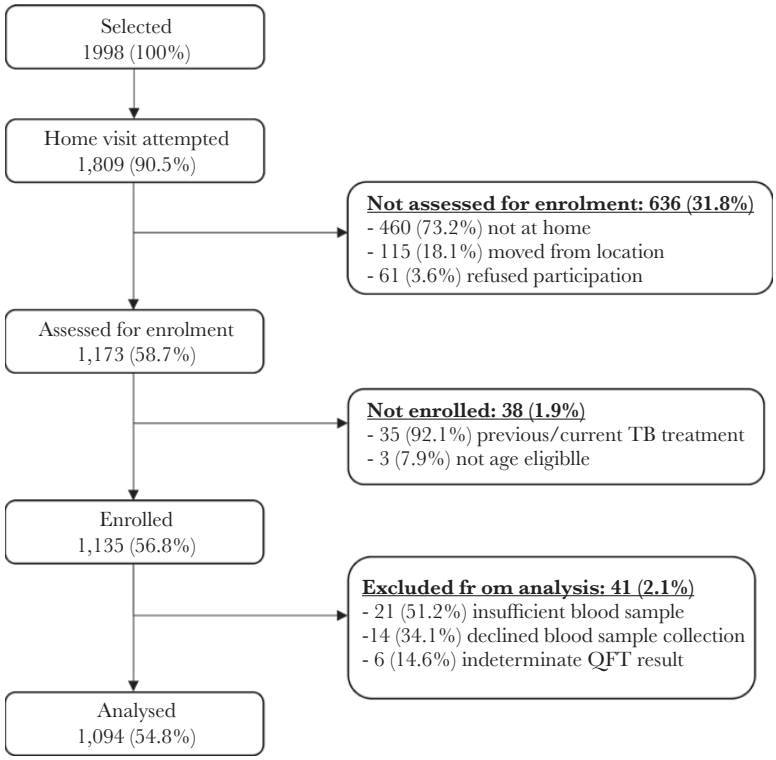

Figure 2 Flow diagram showing participants from selection to analysis.

Risk Factors for *Mycobacterium tuberculosis* Infection

At community level, there was evidence of an association between *M tuberculosis* infection and community HIV prevalence (Table 2). The odds of *M tuberculosis* infection increased with increasing community HIV prevalence (linear OR: 1.43 for each unit increase in community HIV prevalence category).

At the individual level, *M tuberculosis* infection was positively associated with older age and having a lifetime household TB contact (Table 2). The odds of *M tuberculosis* infection increased with increasing age (linear OR: 1.37 for each unit increase in age group) and were 2.1 times higher among participants with history of a household TB contact compared with those without. There was no evidence of association between *M tuberculosis* infection and BCG vaccination or HIV infection after adjusting for community, household, and individual-level factors (Table 2). *Mycobacterium tuberculosis* infection was inversely associated with number of visits to church in the previous month and houses visited during day hours in the previous week. There was no evidence of an association with sharing a sleeping room with other people or with other estimates of social contacts (Table 2).

DISCUSSION

In this high TB/HIV prevalence setting, the prevalence of *M tuberculosis* infection (23.0%) among adolescents was lower than found in the Western Cape province, South Africa [22, 23]. To our knowledge, this is the first study reporting strong evidence of an association between *M tuberculosis* infection and increased community-level HIV prevalence.

Recent data on *M tuberculosis* infection among adolescents largely come from 2 studies in densely populated townships in Western Cape province where prevalence (defined as tuberculin skin test [TST] induration ≥10 mm) was much higher: 37% among 5- to 17-year-olds [23] and 42.2% (95% CI, 40.9–43.6) [22] among 12- to 18-year-olds. Possible explanations for this difference include differences in social contact patterns, because our study was conducted in a less densely populated rural area. A second explanation could be differences in population prevalence of active TB; at the time of the studies in Western Cape (2009), the annual TB notification was approximately 1400 per 100 000 [22, 23] compared with 577 per 100 000 in 2015 for uMkhanyakude district (the setting of our study) [24]. A third possible explanation is differences in HIV prevalence among notified TB patients. For example, in 2015 the HIV prevalence among people notified with TB was 64.3% in uMkhanyakude district compared with 44.6% in Cape Town [24]. At individual level, HIV-positive individuals are likely to be less infectious due to reduced likelihood of cavitary lung disease [25].

A 2013 TST survey among school-going children aged 6–8 years in our setting reported an *M tuberculosis* infection prevalence of 12.4% (95% CI, 10.2%–15.0%) using TST ≥10 mm [26]. The 2013 survey did not find an association between age

Table 1. Characteristics of Study Participants (n = 1094)

Characteristic	N (%)
Sex	
Female	548 (50.1)
Male	546 (49.9)
Age (years)	
10–11	237 (21.7)
12–14	349 (31.9)
15–17	297 (27.2)
≥18	211 (19.3)
Lifetime Household TB Contact (N = 1089)	
No	823 (75.6)
Yes	266 (24.4)
HIV Status	
Negative	855 (78.2)
Positive	43 (3.9)
Unknown	196 (17.9)
BCG Vaccination (N = 1085)	
Vaccinated	984 (90.7)
Not vaccinated	101 (9.3)
Location	
Rural	715 (65.4)
Urban	379 (34.6)
Household Socioeconomic Index Tertiles[a] (1048)	
Low	305 (29.1)
Middle	350 (33.4)
High	393 (37.5)
Number of Household Residents (N = 1070)	
<6	333 (31.1)
6–7	252 (23.6)
8–10	248 (23.2)
>10	237 (22.2)
Church Attendance in Previous 4 Weeks (N = 1073)	
None	664 (61.9)
1–2 times	176 (16.4)
≥3 times	233 (21.7)

Abbreviations: BCG, Bacillus Calmette-Guérin; HIV, human immunodeficiency virus; TB, tuberculosis.

[a]Index scores obtained from a principal component analysis (as described in Supplementary Section 2) were categorized into worth tertiles with the lowest tertile coded "1" and labeled "low socioeconomic status". The highest tertile was coded "3" and labeled "high socioeconomic status".

and community-level HIV prevalence, but the odds of *M tuberculosis* infection were slightly higher (adjusted OR, 1.8; 95% CI, 1.1–3.1) in participants living in households with at least 2 HIV-positive individuals. The higher *M tuberculosis* infection prevalence and the association with increased age in the current study (in older individuals) reflect longer cumulative exposure to people with infectious TB and increased social contact of older adolescents with the wider community [7, 14]. In addition, the older adolescents in our study would also have experienced a higher risk of TB infection in their early lives, because TB notification rates in KwaZulu-Natal have fallen over the last decade [24].

Similar to the Western Cape study [22], we found increased odds of *M tuberculosis* infection among participants with a lifetime household TB contact. Thus, transmission within households of individuals with TB disease remains an important consideration for TB prevention and care programs and highlights the need for enhancing household TB contact tracing to reduce transmission. Despite this, 68% of our participants with *M tuberculosis* infection reported to have never lived in the same house as an individual with TB disease.

The DSA setting of our study allowed us to investigate the effect of the participant's community HIV prevalence on *M tuberculosis* infection. Although ART reduces the risk of TB disease after infection and ART access has improved over the years [27], HIV-positive individuals remain at elevated risk of TB disease [28, 29]. Through long-term, population-based surveillance, we have shown that HIV prevalence has remained consistently high in certain communities within the DSA over several years [19, 27]. We have also shown that active TB, and specifically drug-resistant TB, are associated with those high HIV prevalence areas [30, 31]. The association between higher *M tuberculosis* infection prevalence among adolescents with higher community HIV prevalence suggests possible clustering and continued transmission in these communities. Targeted efforts to find and treat TB in such communities could be effective in reducing *M tuberculosis* transmission. Our findings also support the need for research to explore the feasibility and impact of expanded TB preventive therapy in high transmission areas, in line with World Health Organization recommendations and the South African National Strategic Plan [17, 32].

The odds of *M tuberculosis* infection were lower among participants who reported visiting at least 3 houses during day hours in the previous week and those who attended at least 3 prayer meetings in the previous month. This is likely due to residual confounding. In addition, a recent mathematical modeling suggested that although household and repeated nonhousehold contacts contribute approximately 50% of contact time, they, respectively, contribute to only approximately 13% and 8% of disease transmission, and that approximately 79% of transmission is likely to be from nonrepeated (ie, "casual") contacts [33]. Thus, the apparent protective effect seen in our data from attendance to prayer meetings and visits to other houses could be because the contacts during these visits are likely to be repetitive.

This study has limitations. First, participants from urban communities and communities with high HIV prevalence were underrepresented. Because *M tuberculosis* infection prevalence was higher in communities with HIV prevalence ≥45%, our overall estimate for *M tuberculosis* infection prevalence may have been slightly underestimated. The estimate for *M tuberculosis* infection prevalence may have also been underestimated, because individuals with a history of current or previous TB treatment were excluded. However, this would only give a minor change in the estimate (as shown in Supplementary Section 4). Another limitation is that social contact information was

Table 2. Risk Factors for *Mycobacterium tuberculosis* Infection Showing Odds Ratios Obtained From the Crude, Partial, and Fully Adjusted Models at Each Level of Hierarchical Approach

Variable	QFT Positive n/N (%)	Crude OR (95% CI)	*P* Value	Adjusted OR[a] (95% CI)	*P* Value	Adjusted OR[b] (95% CI)	*P* Value
Community Level Factors							
Community HIV Prevalence (%)							
<25%	12/85 (14.1)						
25%–34.9%	133/618 (21.5)						
35%–44.9%	61/261 (23.4)	1.43 (1.07–1.92)	.02[c]				
≥45%	26/82 (31.7)						
Location							
Rural	156/715 (21.8)	1	.34	1[d]	.54		
Urban	93/379 (24.5)	1.21 (0.81–1.80)		0.84 (0.48–1.47)			
Household Level Factors							
Distance to Nearest Clinic (km) (Quartiles)							
<1.85	84/301 (27.9)	1	.13	1[d]	.21	1[e]	.30
1.85–3.41	80/403 (19.9)	0.56 (0.34–0.92)		0.59 (0.35–1.01)		0.64 (0.36–1.14)	
3.42–5.36	55/259 (21.2)	0.64 (0.38–1.08)		0.78 (0.43–1.42)		0.82 (0.43–1.59)	
>5.36	30/131 (22.9)	0.71 (0.37–1.37)		1.02 (0.50–2.06)		1.21 (0.56–2.65)	
Household Social Economic Index Score (Tertiles)							
Low	74/305 (24.3)	1	.72	1[d]	.75	1[e]	.75
Middle	79/350 (22.6)	0.87 (0.5–1.47)		0.81 (0.46–1.41)		0.81 (0.46–1.41)	
High	83/393 (21.1)	0.81 (0.49–1.36)		0.89 (0.52–1.54)		0.89 (0.52–1.54)	
Number of Residents							
<6	87/333 (26.1)	1	.25	1[d]	.32	1[e]	.41
6–7	58/252 (23.0)	0.83 (0.49–1.41)		0.83 (0.47–1.45)		0.89 (0.48–1.65)	
8–10	50/248 (20.2)	0.62 (0.35–1.09)		0.61 (0.34–1.11)		0.61 (0.32–1.18)	
>10	46/237 (19.4)	0.60 (0.34–1.07)		0.64 (0.35–1.14)		0.65 (0.34–1.24)	
Reported Smoker in Household							
No	197/880 (22.4)	1	.96	1[d]	.53	1[e]	.58
Yes	47/207 (22.7)	0.99 (0.62–1.59)		0.85 (0.50–1.43)		0.85 (0.49–1.50)	
Individual-Level Factors							
Sex							
Female	123/548 (22.4)	1	.85	1[f]	.96	1[g]	.80
Male	126/546 (23.1)	1.04 (0.72–1.50)		0.99 (0.64–1.52)		0.95 (0.62–1.45)	
Age (Years)							
10–11	49/237 (20.7)						
12–14	62/349 (17.8)						
15–17	71/297 (23.9)	1.32 (1.09–1.59)	<.01[c]	1.36 (1.09–1.71)[f,c]	.01	1.37 (1.10–1.71)[g,c]	.01
≥18	67/211 (31.8)						
Lifetime Household TB Contact							
No	168/823 (20.4)	1	.01	1[f]	.02	1[g]	.01
Yes	78/266 (29.3)	1.90 (1.20–3.01)		1.90 (1.12–3.12)		2.13 (1.25–3.64)	
HIV Status							
Negative	193/855 (22.6)	1	.88	1[f]	.39	1[g]	.35
Positive	9/43 (20.9)	0.91 (0.34–2.40)		0.65 (0.20–2.11)		0.65 (0.20–2.09)	
Unknown	47/196 (24.0)	1.11 (0.69–1.81)		1.41 (0.78–2.53)		1.43 (0.80–2.56)	
BCG Vaccination							
Vaccinated	216/984 (22.0)	1	.24	1[f]	.99	1[g]	.65
Not vaccinated	28/101 (27.7)	1.43 (0.78–2.65)		1.00 (0.47–2.15)		1.19 (0.32–2.98)	
Smoking							
No	240/1070 (22.4)	1	.32	1[f]	.81	1[g]	.54
Yes	6/18 (33.3)	1.98 (0.52–7.54)		0.82 (0.17–4.07)		0.61 (0.12–2.26)	
Alcohol Intake							
No	226/1021 (22.1)	1	.21	1[f]	.76	1[g]	.75
Yes	16/54 (29.6)	1.59 (0.72–3.54)		1.17 (0.44–3.06)		1.17 (0.45–3.04))	
Admission to Hospital							
No	221/967 (22.9)	1	.67	1[f]	.40	1[g]	.27

Table 2. Continued

Variable	QFT Positive n/N (%)	Crude OR (95% CI)	*P* Value	Adjusted OR[a] (95% CI)	*P* Value	Adjusted OR[b] (95% CI)	*P* Value
Yes	25/121 (20.7)	0.87 (0.48–1.60)		0.74 (0.37–1.48)		0.68 (0.34–1.36)	
Social Contact Factors							
Contact Hours With Adult Men							
<100	63/274 (23.0)	1	.95	1[f]	.76	1[g]	.69
100–1047	63/275 (22.9)	0.99 (0.58–1.67)		1.30 (0.70–2.43)		1.47 (0.78–2.76)	
1048–2400	59/272 (21.7)	0.89 (0.53–1.52)		1.00 (0.53–1.87)		1.16 (0.62–2.18)	
>2400	64/273 (23.4)	1.04 (0.62–1.76)		1.24 (0.66–2.32)		1.24 (0.66–2.31)	
Contact Hours With Adult Females							
<160	68/277 (24.5)	1	.47	1[f]	.83	1[g]	.89
160–1216	53/274 (19.3)	0.69 (0.41–1.18)		0.80 (0.43–1.49)		0.91 (0.49–1.66)	
1216–2880	66/270 (24.4)	1.03 (0.61–1.74)		1.07 (0.57–2.00)		1.16 (0.63–2.16)	
>2880	62/273 (22.7)	0.89 (0.53–1.50)		0.99 (0.53–1.84)		1.09 (0.59–2.00)	
Church Attendance in Previous Month							
None	165/664 (24.8)	1	.08	1[f]	.13	1[g]	.04
1–2 times	37/176 (21.0)	0.75 (0.44–1.26)		0.66 (0.35–1.23)		0.59 (0.32–1.10)	
≥3 times	41/233 (17.6)	0.58 (0.35–0.95)		0.58 (0.33–1.03)		0.49 (0.27–0.89)	
Health Facility Attendance (12 Months)							
No	142/667 (21.3)	1	.26	1[f]	.88	1[g]	.83
Yes	104/422 (24.6)	1.24 (0.85–1.81)		1.03 (0.66–1.61)		1.04 (0.68–1.62)	
Visiting Other Houses During the Day							
None	169/720 (23.5)	1	.02	1[f]	.02	1[g]	.01
1–2 houses	59/227 (26.0)	1.20 (0.76–1.88)		1.17 (0.69–1.91)		1.00 (0.60–1.69)	
≥3 houses	17/136 (12.5)	0.38 (0.19–0.78)		0.31 (0.13–0.72)		0.28 (0.12–0.66)	
Sharing Sleeping Room With Other People							
None	84/363 (23.1)	1	.88	1[f]	.71	1[g]	.56
1 person	78/336 (23.2)	0.97 (0.61–1.54)		1.24 (0.73–2.11)		1.33 (0.78–2.26)	
≥2 persons	84/389 (21.6)	0.89 (0.57–1.40)		1.08 (0.64–1.83)		1.13 (0.66–1.93)	

Abbreviations: BCG, Bacillus Calmette-Guérin; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio; QFT, QuantiFERON TB-Gold plus; TB, tuberculosis.

[a]Partially adjusted by a priori confounders and variables remaining significant ($P < .2$) at higher levels in the hierarchy.

[b]Adjusted by a priori confounders, variables remaining significant ($P < .2$) at higher levels in the hierarchy, and variables remaining significant ($P < .2$) that levels in the hierarchy.

[c]Odds ratios modeled as a linear trend across the categories; n and % of QFT positive in each category shown for information only.

[d]Adjusted by community HIV prevalence.

[e]Adjusted by community HIV prevalence and socioeconomic status (a priori confounder at household level).

[f]Adjusted by community HIV prevalence, socioeconomic status, and age (a priori confounder at individual level).

[g]Adjusted by community HIV prevalence, socioeconomic status, age, lifetime household TB contact, attendance to church, and visiting other houses during the day.

captured retrospectively by asking participants about their attendance at indoor gathering places and details of the last visit. Although knowledge of attending an indoor gathering place would still be in memory, reporting errors might have been introduced concerning the frequency and duration of visits and numbers of people present, resulting in misclassification that may have obscured associations.

The strength of this study is that we had a large sample size that allowed us to estimate the prevalence with a high precision and gaveus the ability to detect important associations with potential risk factors. We believe that our estimate is reflective of *M tuberculosis* infection prevalence among adolescents in this setting. Moreover, the QFT-plus test was used, which is a more specific test for *M tuberculosis* infection than the TST. Furthermore, we experienced a very low proportion of indeterminate results. Another strength is that this study was nested within in a well defined DSA, which provided a comprehensive sampling frame and allowed us to determine the effect of nonparticipation on the estimate for prevalence.

CONCLUSIONS

In this high TB and HIV burden setting, the prevalence of *M tuberculosis* infection among adolescents was lower than reported from the Western Cape in South Africa. Community-level HIV prevalence, age, and lifetime household TB contact were associated with increased odds of *M tuberculosis* infection. Enhancing TB household contact tracing and targeted active case finding in high HIV prevalence communities has potential to reduce the burden of TB in this setting.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases online*. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility

of the authors, so questions or comments should be addressed to the corresponding author.

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Author contributions. A. D. G., R. L., and K. B. designed the study. T. M., A. S. K., A. E., K. B., and S. R.-R. collected the data. T. M. performed the statistical analyses with oversight from K. B., P. K., and A. D. G. A. T. and F. T. performed analyses for community-level human immunodeficiency virus prevalence. T. M. wrote the manuscript with input from all the authors. All the authors reviewed the manuscript and approved the final version.

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